

Versions with Markings to Show Changes MadeIN THE SPECIFICATION

Please amend the Specification as follows:

Please replace the paragraphs beginning on page 2 at lines 10 and 27 with the following rewritten paragraphs, respectively:

Studies on the physiology of the hypothalamic-pituitary-gonadal axis have resulted in the recognition of gonadotropin releasing hormone (GnRH, otherwise known as luteinizing hormone releasing hormone, LHRH) as a key stimulate the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). More recently, a peptide related to GnRH has been identified, first in chickens (Miyamoto, US Patent no. 4,540,513) and subsequently in humans (White et al., Proc. Natl. Acad. Sci. USA 95 305-309, 1998). This peptide has been called GnRH-II. The sequences of the two peptides (SEQ ID NOS 5 & 6, respectively).

We have now found that GnRH-II is capable of modulating the differentiation of bone precursor cells and inducing the expansion of osteoblast populations. Accordingly, it is an object of the present invention to provide a pharmaceutical composition for the treatment of osteoporosis, which composition is [characterised] characterized by the inclusion of GnRH-II or an analogue thereof. More specifically, the composition includes a peptide according to the sequence (SEQ ID NO: 7).

Please replace the paragraph beginning on page 3 at line 20 with the following rewritten paragraph:

In the first embodiment, the invention as disclosed herein comprises a pharmaceutical composition for increasing bone mass or bone density, or for accelerating bone growth or repair. Preferably, the invention as disclosed herein comprises a pharmaceutical composition for the treatment of osteoporosis (including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis). The

composition is [characterised] characterized in that it includes as an active principal a peptide according to the sequence (SEQ ID NO: 7).

Please replace the paragraphs beginning on page 5 at line 1 and 17 with the following rewritten paragraphs, respectively:

In a second embodiment, the invention disclosed herein comprises a method for the preparation of a pharmaceutical composition for the treatment of osteoporosis (including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis) or another disorder, which method comprises the mixing of a peptide according to the sequence (SEQ ID NO: 7).

In the third embodiment, the invention as disclosed herein comprises a method for the treatment of an individual suffering from osteoporosis (including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis) or another bone disorder, or considered to be at risk of so suffering. This method of treatment comprises the administration to said individual of a therapeutically effective amount of a composition containing, as an active principal, a peptide according to the sequence (SEQ ID NO: 7).

Please replace the paragraph beginning on page 8 at line 7 with the following rewritten paragraph:

1A. Preparation of resin-bound protected peptide (SEQ ID NO: 8).

Please replace the paragraph beginning on page 9 at line 22, with the following rewritten paragraph:

1B. Cleavage and deprotection (SEQ ID NO: 6).

Please replace the paragraph beginning on page 12 at line 51 with the following rewritten paragraph:

Expression of GnRH-I and GnRH-II was determined by RT-PCR using PCR primers outlined in SEQ ID NOS 1-4. The integrity of the cDNA generated was determined by assessing the relative level of actin amplification.

IN THE CLAIMS:

Please amend claims 1, 3, 5, 7, 8, 10, 11 and 12 as follows:

1. (Once Amended) A pharmaceutical composition for the treatment of osteoporosis, including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis, and other disorders of bone metabolism, or for accelerating bone growth or repair, which composition is [characterised] characterized by the inclusion of a peptide (SEQ ID NO: 7).

3. (Once Amended) The pharmaceutical composition according to Claim 1, wherein the peptide (SEQ ID NO: 6) is

pyroGlu-His-Trp-Ser-His-Gly-Trp-Tyr-Pro-Gly-NH₂ (6)

5. (Once Amended) A method of preparing a pharmaceutical composition for the treatment of osteoporosis, including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis, or another disorder of bone growth, which method comprises the mixing of a peptide according to the sequence (SEQ ID NO: 6).

7. (Once Amended) The method of Claim 5, wherein the peptide is (SEQ ID NO: 6)

pyroGlu-His-Trp-Ser-His-Gly-Trp-Tyr-Pro-Gly-NH₂ (6)

8. (Once Amended) A method of treatment of an individual suffering from osteoporosis, including age-related osteoporosis and osteoporosis associated with post-menopausal hormone

status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis, or another disorder of bone growth, or at risk of so suffering, which comprises the administration to said individual of a therapeutically effective amount of a pharmaceutical composition which includes a peptide according to the sequence (SEQ ID NO: 7).

10. (Once Amended) The method of Claim 8, wherein the peptide is (SEQ ID NO: 6)
 pyroGlu-His-Trp-Ser-His-Gly-Trp-Tyr-Pro-Gly-NH₂ (6)

11. (Once Amended) A new use for a peptide according to the sequence (SEQ ID NO: 7)

pyroGlu-His-Trp-Ser-Xaa¹-Gly- Xaa²- Xaa³-Pro-Gly-NH₂ (7)

or a salt thereof

wherein Xaa¹ is His or Tyr,

Xaa² is Trp or Leu, and

Xaa³ is Tyr or Arg,

Provided that when Xaa¹ is Tyr and Xaa² is Leu, then Xaa³ is not Arg,

which use is as a therapeutic agent for the treatment of osteoporosis, including age-related osteoporosis and osteoporosis associated with post-menopausal hormone status, primary and secondary hyperparathyroidism, disuse osteoporosis, diabetes-related osteoporosis, and glucocorticoid-related osteoporosis, and other disorders of bone growth.

12. (Once Amended) A new use for a peptide according to the sequence (SEQ ID NO: 6)
 pyroGlu-His-Trp-Ser-His-Gly-Trp-Tyr-Pro-Gly-NH₂ (6)

which use is as a therapeutic agent for the treatment of osteoporosis and other disorders of bone growth.